REMARKS

AMENDMENTS TO THE SPECIFICATION

The specification has been amended in the interest of clarity and to correct typographical and grammatical errors. These amendments do not add new matter as detailed below. Entry of these amendments is respectfully requested.

Specification Amendments Beginning on Page 4, Line 8, and Ending on Page 6, Line 4.

The phrase "compounds of the structure" has been removed and replaced with "compounds of Formula I" for clarity. This sentence now clearly refers to the labeled Formula I below.

The phrase "or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof," has been moved from the end of the definitions for the compounds of Formula I to the beginning of the definitions for clarity. This phrase has also been amended to correct grammatical error. The phrase now refers to the plural form of the noun, stating "or pharmaceutically-acceptable salts, optical isomers or prodrugs thereof."

The definition for R^1-R^5 has been amended to clarify the definition for the group of Formula II. The proviso that one of R^1 or R^3 must be selected from a group of Formula II has been placed below this formula in the claim.

The definition of R^{10} and R^{11} for the compounds of Formula I has been amended for clarity. In particular, the expressions "may be joined" and "said ring being optionally substituted" have been amended and the terms "unsubstituted" and "substituted" have been added to clarify that the heterocycle ring is unsubstituted or substituted. The definition of R^{10} and R^{11} now states ". . . R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R^{13}, ..."

The definition of A has been amended to clarify that the aryl and heterocyclyl groups can be either unsubstituted or substituted. The phrase "hydrogen" has accordingly been deleted from the list of substituents for R^{12}.

These amendments are made for clarity and/or to correct typographical errors and do not add new matter.

Specification Amendments Beginning on Page 6, Line 18, and Ending on Page 8, Line 16.

The phrase "compounds of the structure" on page 6, line 18 has been removed and replaced with "compounds of Formula III" for clarity. This sentence now clearly refers to the labeled Formula III below.

The phrase "D, B, Y, and Z are as defined above" on page 7, line 5 has been amended to recite "D, B, Y, and Z are as defined above for Formula I," to clarify that this phrase refers to Formula I.

The R^{12} definitions on pages 7 and 8 for Formulas III and IV, respectively, have been amended to delete the hydrogen substituent for consistency with the amendments to the R^{12} definition for Formula I, as described above.

The R^{10} and R^{11} definitions on pages 7 and 8 have been amended as described above for the amendments to the definitions for Formula I.

The phrase "compounds of the structure" on page 7, line 18 has been removed and replaced with "compounds of Formula III" for clarity. This sentence now clearly refers to the labeled Formula IV below.

These amendments are made for clarity and/or to correct typographical errors and do not add new matter.

Specification Amendments Beginning on Page 28, Line 10, and Ending on Page 31, Line 10.

The specification, page 28, lines 10-14, has been amended slightly in the interest of clarity. In particular, the term "ring" has been added to line 10, to refer to the oxazole ring shown in Scheme 1. The sentence "In Scheme 1, and likewise in Schemes 2 and 4, the substituent X is a leaving group" has been added. The new sentence describes Schemes 1, 2, and 4 which all contain aryl methyl ketone **1**. The terms (R_{1-2}, and R_{4-5}) have been added to describe the substitution as seen on aryl methyl ketone **1** in Scheme 1 (amended as described below). The number **2** has been added after the term "Biarylsulfide," to refer to the biarylsulfide shown in Scheme 1. The term "oxazole" has been added to line 14 in reference to compound **4**, shown in Scheme 1, as an oxazole compound. The above-described amendments merely clarify the invention as described in the specification and shown in Schemes 1, 2, and 4 and no new matter is added by these amendments.

The description of Schemes 1-6, on pages 28-31 of the specification has also been amended to correct obvious typographical and/or grammatical errors. In particular, the plural form for referencing a compound structure has been changed to the singular form, when a single compound structure is described. The above amendments merely correct typographical and/or grammatical errors and clarify the invention as described in the specification and shown in Schemes 1-6.

Schemes 1-6 have been amended to correct obvious typographical errors in the interest of clarity. Specifically, the R_{1-4} group in these schemes is now represented by two groups, R^{1-2}, and R^{4-5}, and the Ar group lettering has been changed to A. The R group numbering and A group lettering is now consistent with the numbering and lettering shown in Formula I, on page 4, line 9 of the Specification, and in Claim 1, p. 121, line 4. Schemes 1-6 have also been amended such that the numbering of NR_9R_{10} is changed to $NR^{10}R^{11}$. This R group numbering is now consistent with the numbering shown in Formula II, on page 4, line 14 of the Specification, and in Claim 1, p. 121, line 10. Scheme 6 has further been amended such that Compound **22** is consistent with the remainder of Scheme 6. Specifically, the CF_3 group in Compound **22** has been changed to R^{1-2} and R^{4-5} groups. Compound **22**, as amended,

is consistent with the preceding compound structures in Scheme 6, and is also consistent with Formula I, as shown on page 4, line 9 of the Specification, and in Claim 1, p. 121, line 4.

The above amendments to the Specification correct obvious errors. Accordingly, no new matter is added by these amendments. The Applicants respectfully request that the above-described amendments be entered into the application.

AMENDMENTS TO THE CLAIMS

This Response and Amendment amends Claims 1-9 and adds new Claims 10-27. These amendments and new claims do not add new matter as detailed below. Entry of the amendments and new claims is respectfully requested.

Claim 1.

Claim 1 has been amended such that the phrase "A compound of the structure" has been removed and replaced with "A compound of formula I," and the formula below has been labeled "I" for clarity. This preamble of Claim 1 now clearly refers to the labeled formula I below.

The phrase "or a pharmaceutically-acceptable salt or prodrug thereof," has been moved from the end of the definition for the compounds of formula I to the beginning of the definition for clarity. The phrase "or optical isomer" has been removed from Claim 1 for clarity. Formula I, as written, and the subsequent definitions, represents all of the optical isomers. Thus, the phrase "or optical isomer" has been removed as it is clearly redundant.

The definition for R^1-R^5 has been amended to clarify the definition for the group of formula II, and formula II has been labeled accordingly. The proviso that "one or more than one of R^1 or R^3 is a group of formula II . . ." is now appropriately below formula II, as defined above.

The definition for R^{10} and R^{11} in Claim 1 has been amended for clarity. In particular, the term "or" has been added to the end of the definition for R^{10} and R^{11}. In

addition, the expressions "wherein R^{10} and R^{11} may be joined . . ." and "said ring being optionally substituted" have been amended and the terms "unsubstituted" and "substituted" have been added to clarify that the heterocycle is unsubstituted or substituted. The definition of R^{10} and R^{11} now states "R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R^{13}, ..."

The definition of A in Claim 1 has been amended to clarify that the aryl and heterocyclyl groups can be either unsubstituted or substituted. The phrase "hydrogen" has accordingly been deleted from the list of substituents for R^{12}.

Claim 2.

Claim 2 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 1 wherein R^3 is" to "A compound according to claim 1 wherein R^3 is the group of formula II." The phrase is amended to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to the preceding independent claim. The formula in Claim 2 has appropriately been labeled "II." In addition, the definitions for D, B, Y, Z, R^{10} and R^{11} in Claim 2 have been amended to clarify that these substituents are defined as in claim 1. The additional Claim 2 definitions have been deleted and are defined as in Claim 1.

Claim 3.

Claim 2 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 1 of the structure" to "A compound according to claim 1 of formula III." The phrase is amended to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to the preceding independent claim. The formula in Claim 3 has appropriately been labeled "III." In addition, the definitions for R^1, R^2, R^4, R^5, R^{10}, R^{11}, R^{12}, D, B, Y, Z, and n in Claim 3 have been deleted and are defined as in Claim 1.

Claim 4.

Claim 4 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 3 . . ." to "A compound according to claim 3 . . ." The phrase is amended to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to the preceding claims, upon which Claim 4 depends. The definition for R^{10} and R^{11} in Claim 4 has been amended for clarity as described in the amendment to Claim 1 above. The phrase "wherein R^{10}, R^{11}, R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group" has been added to clarify that these groups, (*i.e.*, the substituents redefined in Claim 4), can be unsubstituted or substituted. Support for this amendment is found in Claim 1 as originally filed.

Claim 5.

Claim 5 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 1 of the structure" to "A compound according to claim 1 of formula IV." The phrase is amended to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to the preceding claims, upon which Claim 5 depends. The formula in Claim 5 has appropriately been labeled "IV." The definitions for R^{10} and R^{11} in Claim 5 have been amended and are defined as in Claim 1. The phrase "wherein R^{12} is unsubstituted or substituted with at least one electron donating group or electron withdrawing group" has been added to the R^{12} definition, which is redefined in Claim 5. Accordingly, the phrase "wherein R^1, R^2, R^4, R^5, R^{10}, R^{12}, and R^{13}, are unsubstituted or substituted . . ." has been deleted from Claim 5. Support for this amendment is in Claim 5, as originally filed. The phrase "hydrogen" has been deleted from the definition of R^{12}, as is consistent with the amendments to Claim 1.

Claim 6.

Claim 6 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 5 . . ." to "A compound according to claim 5 . . ." The phrase is amended to clarify that the claim includes "pharmaceutically acceptable salts or

prodrugs" according to the preceding claims, upon which Claim 6 depends. The definition for R^{10} and R^{11} in Claim 6 has been amended for clarity as described in the amendment to Claim 1. The definition for R^{12} has been deleted from Claim 6 and is now inherently defined as in Claim 5, upon which Claim 6 depends.

Claim 7.

Claim 7 has been amended to recite a clear dependent claim format by changing the phrase "The compound of claim 1 . . ." to "A compound according to claim 1 . . ." to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to preceding Claim 1, upon which Claim 7 depends.

Claim 8.

Claim 8 has been amended to recite clear dependent claim format as described in the amendment to Claim 7 above. Claim 8 has also been amended such that the phrase "in a pharmaceutically acceptable carrier" is now correctly recited as "and a pharmaceutically acceptable carrier."

Claim 9.

Claim 9 has been amended to recite a clear dependent claim format by deleting the phrase "of" and adding the phrase "according to" to clarify that the claim includes "pharmaceutically acceptable salts or prodrugs" according to preceding claim 1, upon which Claim 9 depends.

Claim 10.

Support for Claim 10 is found in the specification on page 11, lines 3-7: "The term "aryl" . . . refers to a mono. . . cyclic carbocyclic ring system having one or two aromatic rings. . . optionally substituted . . . ." Further support for Claim 10 is found in the specification on page 6, lines 6-12, which states "A is an aryl or heterocyclyl group, having at least one substituent R^{12}, . . ." and on page 14, lines 3-6, which states that

[h]eterocyclics also include compounds of the formula (shown in the specification), where X* and Z* are independently selected from. . . -CH_2-. . . -NH- and -O-, with the proviso that at least one of X* and Z* is not -CH_2, and Y* is selected from. . . and -$(C(R'')_2)_v$-, where R'' is hydrogen or alkyl of 1 to 4 carbons, and v is 1-3.

Claim 11.

Support for Claim 11 is found in the specification on page 11, lines 3-7.

Claim 12.

Support for Claim 12 is found in the specification on page 6, line 19. Further support for Claim 13 is found in Examples 1-75 on pages 31-96 of the specification

Claim 13.

Support for Claim 13 is found in the specification on page 4, lines 16-17 through page 5, lines 1-2 and in Claim 1, as originally filed on page 121, lines 11-14 of the specification. Further support for Claim 13 is found on pages 28-31 of the specification (e.g., Schemes 1-6) and Examples 1-96 on pages 31-113 of the specification.

Claim 14.

Support for Claim 14 is shown in Schemes 1-6 on pages 28-31 of the specification and Examples 1-96 on pages 31-113 of the specification.

Claim 15.

Support for Claim 15 is found in the specification on page 4, lines 16-17 through page 5, lines 1-2 and in Claim 1, as originally filed on page 121, lines 11-14 of the specification. Further support for Claim 15 is shown in Schemes 1-3, on pages 28-29 of the specification and in Examples 1-13, on pages 31-44 of the specification.

Claim 16.

Support for Claim 16 is found in the specification on page 4, lines 16-17 through page 5, lines 1-2 and in Claim 1, as originally filed on page 121, lines 11-14. Further support for Claim 16 is shown in Examples 13-96 on pages 44-113 of the specification.

Claim 17.

Support for Claim 17 is found in the specification on page 4, lines 16-17 through page 5, lines 1-2; page 6, lines 15-17; and in Claim 1, as originally filed on page 121, lines 11-14 of the specification. Further support for Claim 17 is found on pages 28-31 of the specification (e.g., Schemes 1-6) and Examples 1-96 on pages 31-113 of the specification.

Claim 18.

Support for Claim 18 is found in the specification on page 4, lines 11-12 and in Claim 1, as originally filed on page 121, lines 6-7 of the specification. Further support for Claim 18 is found in Examples 1-96 on pages 31-113 of the specification.

Claim 19.

Support for Claim 19 is found in the specification on page 4, lines 11-12 and page 4, lines 16-17 through page 5, lines 1-2, and in Claim 1, as originally filed on page 121, lines 6-7 and 11-14 of the specification. Further support for Claim 19 is found on pages 28-31 of the specification (e.g., Schemes 1-6) and Examples 1-96 on pages 31-113 of the specification.

Claim 20.

Support for Claim 20 is found in the specification on page 4, lines 11-12 and in Claim 1, as originally filed on page 121, lines 6-7 of the specification. Further support for Claim 20 is found on page 13, lines 2-3 of the specification; pages 28-31 of the specification (e.g., Schemes 1-6); and Examples 1-96 on pages 31-113 of the specification.

Claim 21.

Support for Claim 21 is found in the specification on page 5, lines 3-4 and in Claim 1, as originally filed on page 121, lines 15-16 of the specification. Further support for Claim 2 is found in Examples 1-96 on pages 31-113 of the specification.

Claim 22.

Support for Claim 22 is found in the specification on page 4, lines 11-12 and in Claim 1, as originally filed on page 121, lines 6-7 of the specification. Further support for Claim 21 is found in Examples 1-96 on pages 31-113 of the specification.

Claim 23.

Support for Claim 23 is found in the specification on page 4, lines 11-12; and page 13, lines 1-3; and in Claim 1, as originally filed on page 121, lines 6-7 of the specification. Further support for Claim 23 is found in Examples 1-10 on pages 31-41 of the specification.

Claim 24.

Support for Claim 23 is found in the specification on page 4, lines 11-12; and page 13, lines 1-3; and in Claim 1, as originally filed on page 121, lines 6-7 of the specification. Further support for Claim 24 is found in Examples 11-12 on pages 42-44 of the specification.

Claim 25.

Support for Claim 25 is found in the specification on pages 114, line 2 through page 116, line 8, in particular on page 115, lines 3-4.

Claim 26.

Support for Claim 26 is found in the specification on page 4, lines 1-3.

Claim 27.

Support for Claim 27 is found in the specification on page 4, lines 3-6.

The amendments to claims 1-9, as described above, have been made for clarity and/or to correct typographical and grammatical errors. These amendments do not add new matter as described above. New claims 10-27 do not add new matter. Support in the specification and claims, as originally filed, for new claims 10-27 has been detailed above. Accordingly, entry of the amendments to claims 1-9, and new claims 10-27 is respectfully requested.

RESPONSE TO THE RESTRICTION REQUIREMENT

Claims 1-9 are pending in the application and subject to a restriction requirement under 35 U.S.C. § 121 as stated in numbered paragraphs I-V on page 2 of the Office Action mailed June 21, 2002. Applicants respectfully traverse the present restriction requirement as improper under US Patent Office practice and procedure for the restriction of a Markush-type claim. Applicants request reconsideration and withdrawal of the restriction requirement based on the following remarks.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, Applicants propose that the claims be divided into alternate restriction Groups A-D, as detailed below.

A. Restriction Is Improper Because There is Unity Of Invention.

In the present Office Action, the Examiner has identified five groups of compounds that restrict Applicants' invention, as provided in numbered paragraphs I-V thereof (Office Action, page 2). The Office requires restriction on the basis that the inventions are "distinct" and that the inventions "have acquired separate status in the art as shown by their different classification" (Office Action, page 3, lines 18-19). In support of the restriction requirement, the Office asserts that

> [S]eparate searches in the literature as well as in the U.S. Patent Classification System would be required. Each group's compounds are made and used independently of each other and

> could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structure equivalents of each other.

Office Action, page 3, lines 7-10.

Under MPEP § 803.02, restriction of a Markush-type claim is improper, even where the claims are directed to what would otherwise be considered independent and distinct inventions, if the subject matter of the claim has unity of invention. As stated in MPEP § 803.02, "unity of invention exists where compounds included within a Markush Group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

Applying the standard set forth in the US Patent Office guidelines for the examination of Markush claims, the present restriction requirement is improper because the compounds of the present invention do in fact have clear unity of invention. In particular, the compounds: (1) share a common utility (*i.e.*, they are LFA-1 antagonists); and (2) share a structural feature essential to the common utility, (*i.e.*, they are all phenyl sulfide heterocyclyl "amino" (e.g., $NR^{10}R^{11}$) compounds and the linking sulfide and "amino" are required for utility).

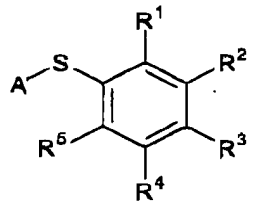
1. Applicants' Compounds Have A Common Utility

Applicants' claimed compounds have a common utility (*e.g.*, they are LFA-1 antagonists). The specification asserts that these compounds bind to the I-domain of LFA-1 and block the interaction of LFA-1 to ICAMs. Applicants' compounds are useful for the treatment of diseases such as inflammatory diseases, autoimmune diseases, tumor metastasis, allograft rejection, and reperfusion injury. Specification, page 4, lines 1-6. The utility Applicants' compounds is demonstrated by the *in vitro* testing described in Examples 97A and 97B of the specification on pages 113-116. Specifically, the compounds of the invention "inhibit the binding of ICAM-1 to LFA-1 with an IC_{50} of less than 20 micromolar." (Specification, page 115, lines 3-4.)

2. Applicants' Comp unds Have Common Structural Features Essential to the Asser ed Utility.

Applicants' claimed compounds share a structural feature essential to the common utility, (*i.e.*, they are all phenyl sulfide heterocycle "amino" compounds and the linking sulfide and amine are required for utility). Under, *In re Harnich*, claimed compou nds are part of a single invention and a Markush grouping is proper where there is "a single structural similarity," and the "claimed compounds all belong to a subgenus . . . which is ot repugnant to principles of scientific classification." *In re Harnich*, 206 USPQ 300, 631 F 2d 716, 721 (CCPA 1980), submitted herewith.

Formula I, representing Applicants' claimed compound genus, is shown bel w.



Formula I

Formula I above shows that each compound within Applicants' claimed compound genus has a common phenyl sulfide structure. Further, Applicants claimed compounds each have an "amino" moiety, *e.g.*, an $NR^{10}R^{11}$ group, as shown in Formula I (*see*, e.g., Specification, page 4, line 14). Thus, Applicants' invention comprises not only a "single structural similarity," as required under *In re Harnisch*, but two. Accordingly, th compounds within Applicants' invention can be appropriately classified and searched toget er.

Further, it is Applicants' position that the common phenyl sulfide structure, and "amino" moiety, are essential to the asserted utility of the compounds. The present inven on discloses a series of aryl phenyl sulfide "heterocyclyl" amino compounds. In the *Expert O in. Ther. Patents* article to Liu, G. (submitted to the US PTO in the Supplemental Informatio

Disclosure Statement and accompanying PTO Form 1449, dated April 2, 2002), a number of diaryl sulfide species, including an earlier discovered diaryl sulfide anilino compound, are identified. *See*, Liu, G., *Expert Opin. Ther. Patents* (2001) 11(9):1387. This article specifies that both the sulfide and the anilino group are required for the affinity that results in the utility of the compounds as LFA-1 antagonists.

Although examination of Applicants' claimed invention may involve searching in multiple subclasses, this is not the test for an appropriate restriction requirement for Markush-type claims. Provided that the Markush group has "common utility" and a "common structural feature," essential to that utility, as is the case here, the Markush group is proper under the Patent Office guidelines. MPEP § 803.02. Accordingly, Applicants respectfully request reconsideration and withdrawal of the Restriction/Election requirement.

B. The Restriction Requirement Is Improper For Groups That Are Classifiable Together.

In the present Office Action, Applicants' invention is restricted into Groups III and IV, which are both classified in class 548. Restriction of an invention that is classified together is improper, unless the Office provides evidence of separate status in the art, and also a separate field of search. Where the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions. MPEP § 808.02.

In the present case, the Office has not provided any evidence of separate status in the art for Groups III and IV, and has not indicated that a different field of search is required. In support of the restriction requirement, the Office states that "each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structure equivalent of each other."

In response, Applicants would like to point out that Groups III and IV both contain 5-membered heterocycles containing 1 N atom and another heteroatom, either O or S

(representing oxazoles and thiazoles, respectively). Further, Scheme 1 and Scheme 3 in the specification, pages 29-30, clearly shows that the compounds within Groups III and IV can be formed from the same intermediate compound (*i.e.*, compound **3**), in similar synthetic procedures, which employ different reagents, to arrive at either the desired oxazole compounds (*e.g.*, compound **4**), or thiazole compounds (*e.g.*, compound **10**).

The Office also states that the "inventions are distinct for the reasons given above and have acquired separate status in the art as shown by their different classification." Office Action, page 3. This assertion is clearly without basis as applied to Groups III and IV, as these Groups have the same classification, *i.e.*, Class 548.

Thus, given that the compounds within Groups III and IV have the same classification within the U.S. Patent Classification System, similar chemical structures, and similar synthetic preparations, the Office has clearly not met the burden of showing evidence of separate status, or a separate field of search, as required for proper restriction. Applicants request withdrawal of the restriction requirement on this basis.

C. Proposed Election/Restriction Requirement

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, Applicants propose that the claims be divided into the following Groups A-D.

A. Claims 1-14, and 16-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 6- membered heterocycle containing 2 N atoms, classified in class 544.

B. Claims 1-14, and 16-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 6- membered heterocycle containing 1 N atom, classified in class 546, subclass various.

C. Claims 1-15, and 17-27 (in part), drawn to compounds, compositions, methods of use, and processes of making compounds, where R^1 or R^3 is a 5- membered

heterocycle containing 1 N atom and another heteroatom, classified in class 548, subclass various.

D. Claims 1-27 (in part), drawn to others, classified in various classes and subclass various.

Although Applicants do not agree with the propriety of an Election/Restriction requirement at this time, to advance prosecution of this case, alternate Groups A-D are proposed above. In view of the common structural features and common utility of the compounds of the present invention, as discussed above, and the common classification, the Examiner is urged to accept the above-proposed restriction/election. If the above-proposed restriction/election is not at this time acceptable to the Examiner, the Applicants respectfully request further discussion regarding the restriction of the invention under 35 U.S.C. §121.

D. Provisional Election.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, and the Examiner accepts the alternate Election/Restriction Groups A-D above, Applicants provisionally elect, with traverse, Group A. Claims 1-14, and 16-27 are readable on Group A.

If, notwithstanding Applicants' present request for reconsideration, the Examiner maintains that an Election/Restriction Requirement of some nature should be made, and the Examiner does not accept the alternate Election/Restriction Groups A-D above, Applicants provisionally elect, with traverse, Group I. Claims 1-14, and 16-27 are readable on Group I.

CORRESPONDENCE ADDRESS.

Initially, it is noted that the Office Action mailed June 21, 2002 was sent to the law firm of Marshall Gerstein & Borun. The undersigned attorney requests that the Examiner address all communications to Jeffrey G. Sheldon, Esq., of Sheldon & Mak, 225 South Lake

Avenue, 9th Floor, Pasadena, California 91101, as directed in the Declaration and Power of Attorney Form filed with the US Patent and Trademark Office on April 2, 2002.

CONCLUSION

If there are any issues that can be resolved by telephone with the Applicants representative, the Examiner is encouraged to contact the undersigned directly.

The Commissioner is hereby authorized to charge payment of $434 ($130 for the one month extension and $324 for the additional claim fees) to Deposit Account No. 19-2090. The Commissioner is further authorized to charge any other fees or credit any overpayment associated with this Response and Amendment to Deposit Account No. 19-2090.

Respectfully Submitted,

SHELDON & MAK
a Professional Corporation

Date: 8/21/02

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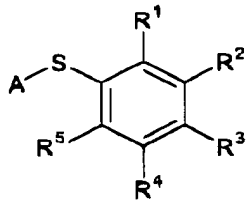
SPECIFICATION AMENDMENTS WITH MARKINGS TO SHOW CHANGES

Beginning n page 4, line 8 and ending on page 6, line 14:

The present invention is directed to compounds of [the structure] Formula I

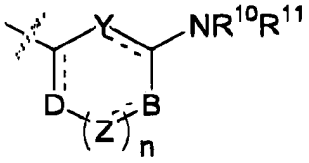


Formula I

or pharmaceutically acceptable salts, optical isomers, or prodrugs thereof,

wherein R^1, R^2, R^3, R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, [and] carboxaldehyde[;], and a group of Formula II defined as;

[with the proviso that at least one of R^1 or R^3 is]



Formula II

subject to the proviso that one or more than one of R^1 or R^3 is a group of Formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of $-CR^6=$, $-CR^7R^8-$, C(O)-, -O-, $-SO_2-$, -S-, $-N=$, and $-NR^9-$;

n is an integer of zero to three;

R^6, R^7, R^8, and R^9, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl[]alkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

[wherein] R^{10} and R^{11} are taken together with N [may be joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, [said ring being optionally] substituted with one or more than one substitutent [substituents] R^{13}, wherein R^{13}, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

wherein A is an unsubstituted aryl [or] group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than [said aryl or heterocyclyl group having at least] one substituent R^{12}, wherein R^{12}, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl,

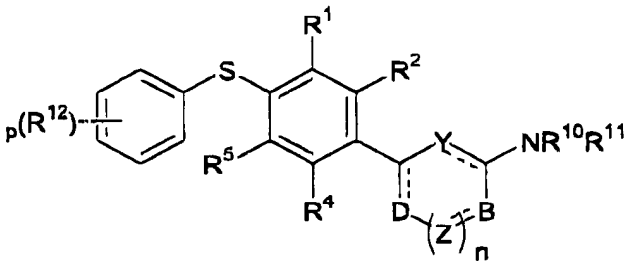
heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamide, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino, and heterocyclylalkylaminocarbonyl; and

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10},R^{11}, R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group;

[or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof].

Beginning on page 6, line 18 and ending on page 8, line 16:

The present invention is also directed to compounds of [the structure] Formula III



Formula III

wherein R^1, R^2, R^3, R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

D, B, Y and Z are as defined above for Formula I;

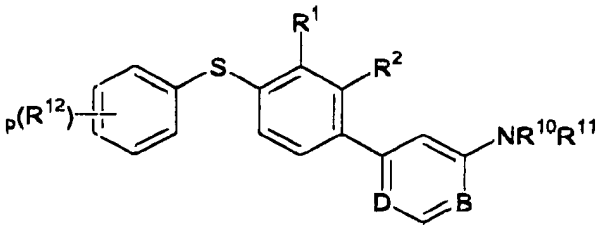
R^{12}, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl; and[,]

p is an integer of zero to five;

wherein R^1, R^2, R^4, R^5, R^{10}, R^{11} and R^{12} are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

Presently most preferred, but not required, compounds of Formula III have p as one; R^4 and R^5 as hydrogen; R^{12} as halogen, alkyl, carboxyalkoxy, carboxyalkyl or heterocyclyl; and R^{10} and R^{11} [joined] are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Presently most preferred, but not required, compounds are of [the structure] Formula IV



Formula IV

wherein D and B are each independently selected from the group consisting of -N= and -CR^6=;

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are as defined above for Formula I;

R^{12}, at each occurrence, is independently selected from the group consisting of [hydrogen], halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

p is an integer of zero to five; and[,]

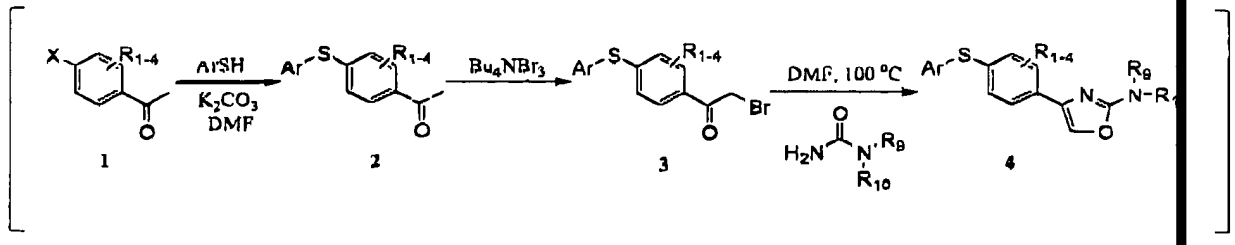
wherein R^1, R^2, R^{10}, R^{11}, and R^{12} are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

[For presently] Presently most preferred, but not required, compounds are of Formula IV, where p [may] can be one; R^{12} [may] can be halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl or heterocyclyl; and R^{10} and R^{11} [may] can be [joined] taken together with N to form a three to seven membered heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

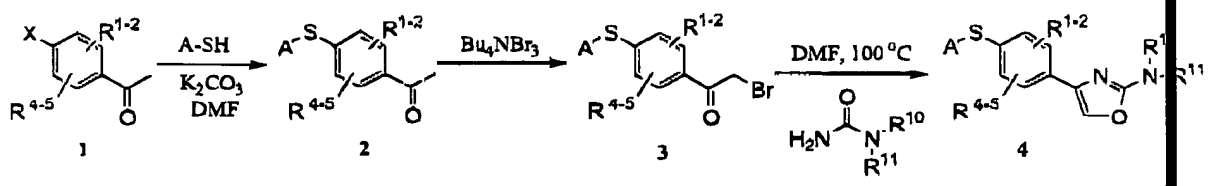
Beginning on page 28, line 10 (with the words "Scheme I"), and ending on page 31, line 10:

Scheme [I] 1 describes compounds of Formula I which contain an oxazole ring (n=0, Y=N, B=O, D=C). In Scheme 1, and likewise in Schemes 2 and 4, the substituent X is a leaving group. In Scheme I, aryl [Aryl] methyl ketone 1, with [the] an appropriate substitution ($R_{1\text{-}2}$ and $R_{4\text{-}5}$), and a leaving group X, reacts with an aryl thiol to give a biaryl sulfide 2. Biarylsulfide 2 can be converted into an alpha-bromomethyl ketone 3 using a variety of reagents including Bu_4NBr_3. Condensation of 3 with a urea [then] gives a [the] desired [compounds] oxazole compound 4.

Scheme 1

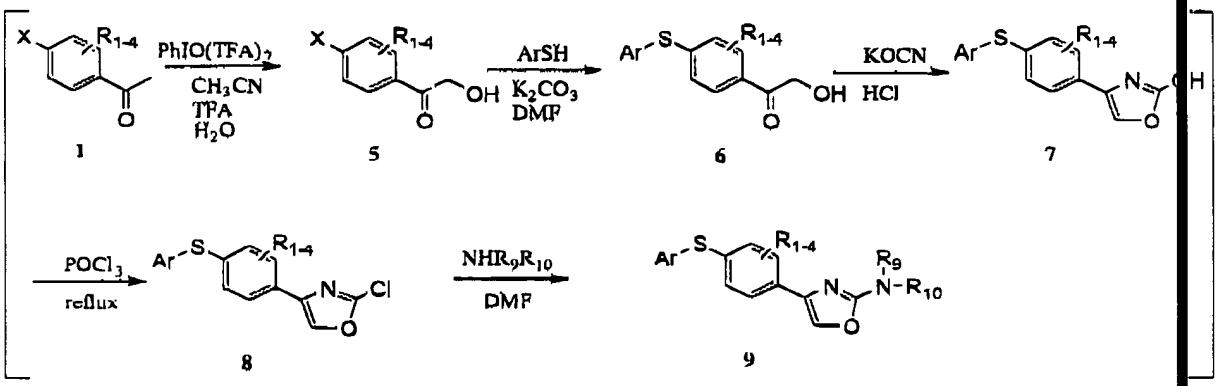


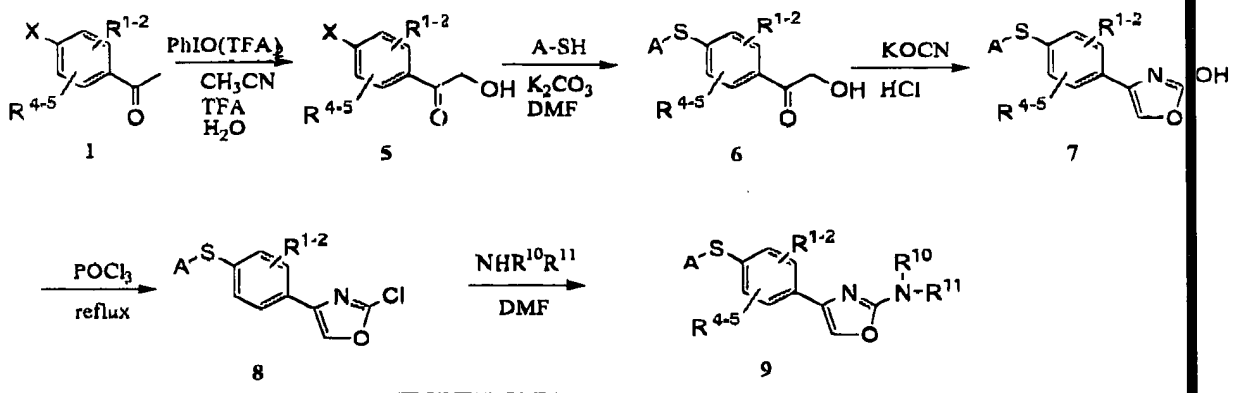
1 2 3 4



Another method of preparing compounds of Formula I containing an oxazole ring (n=0, Y=N, B=O, D=C) is illustrated in Scheme 2. In Scheme 2, an aryl [Aryl] methy ketone [ketones] 1 is [1 are] converted into an alpha-hydroxymethyl ketone **5**, which then can be reacted with an arylthiol [arylthiols] to give a biaryl sulfide **6**. Acid-catalyzed condensation of **6** with KOCN affords a 2-hydroxy oxazole **7**, which can be converted into a 2-chloro-oxazole **8** using $POCl_3$. Displacement of the chloride of **8** with an amine [amines] gives a [the] desired 2-amino-oxazole **9**.

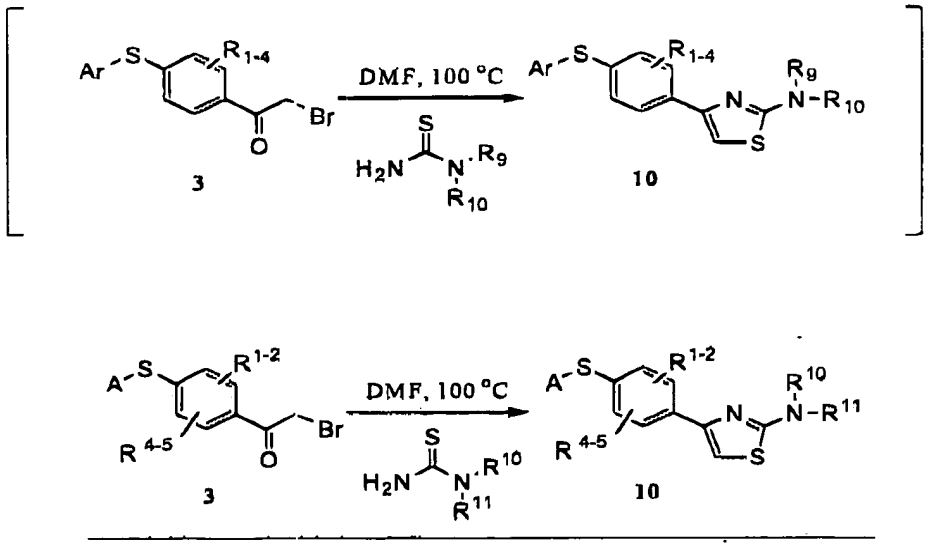
Scheme 2





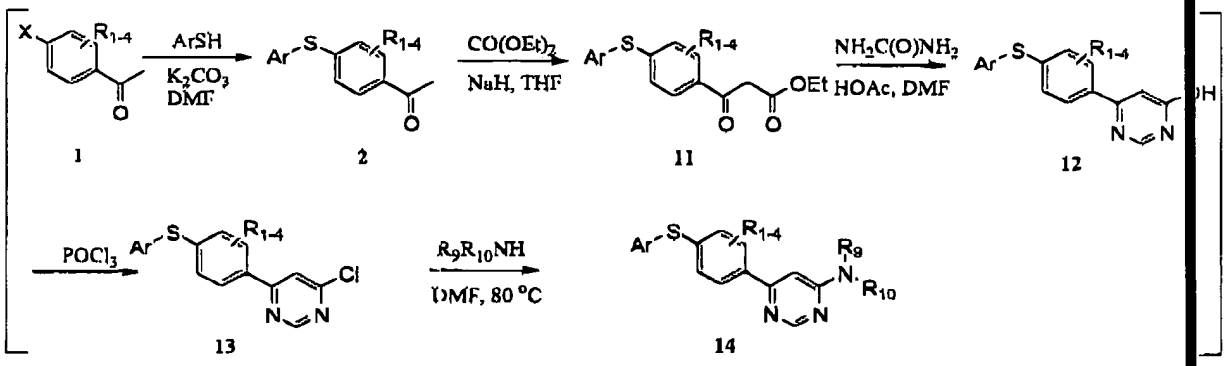
Scheme 3 describes the synthesis of a class of compounds of Formula I containing a thioazole ring (n=0, Y=N, B=S, D=C). In Scheme 3, [The] biaryl sulfide alpha-bromomethyl ketone **3** can be prepared following the procedure outline in Scheme 1. Condensation of **3** with a properly substituted thiourea gives a [the] desired 2-aminothioazole **10**.

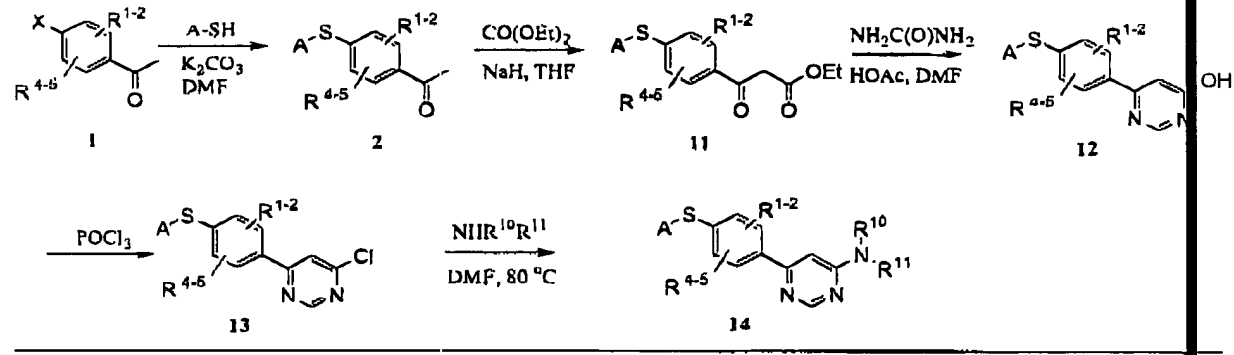
Scheme 3



Another class of compounds of Formula I are compounds containing pyrimidine ring, for example 4,6-disubstituted pyrimidines (n=1, Y=C, B=N, Z=C, D=N). Scheme 4 describes one procedure for the preparation of this class of compounds. Reaction of a biaryl sulfide methyl ketone **2** with diethyl carbonate under base-catalysis leads to a beta-ketoester **11**. Condensation of **11** with formamidine gives a 4-hydroxy pyrimidine **12**, which can be converted into 4-chloropyrimidine **13**. Displacement of the chloride of **13** by amines then gives the desired 4-amino-pyrimidine **14**.

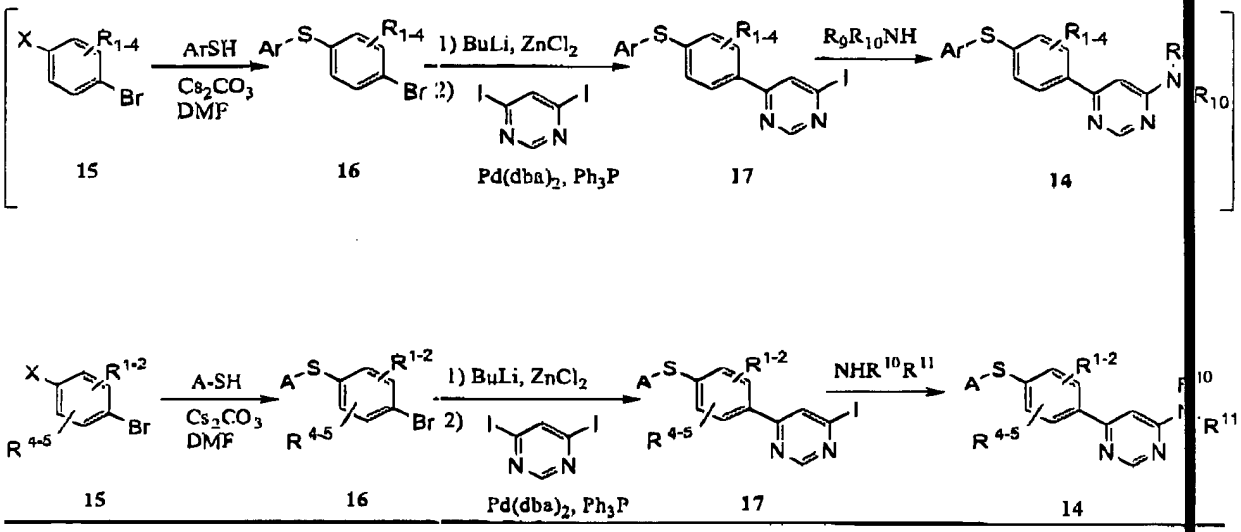
Scheme 4





An alternative synthesis of the 4,6-disubstituted pyrimidines is illustrated in Scheme 5. In Scheme 5, nucleophilic [Nucleophilic] substitution of an aryl fluoride **15** with an aryl thio under base-catalysis gives a biaryl sulfide **16**. Transmetallation of **16** with n-BuLi/$ZnCl_2$, followed by Pd-catalyzed cross-coupling with 4,6-diiodopyrimidine leads to iodopyrimidine **17**. Reaction of **17** with a selected amine [amines] gives a [the] desired 4-aminopyrimidine **14**.

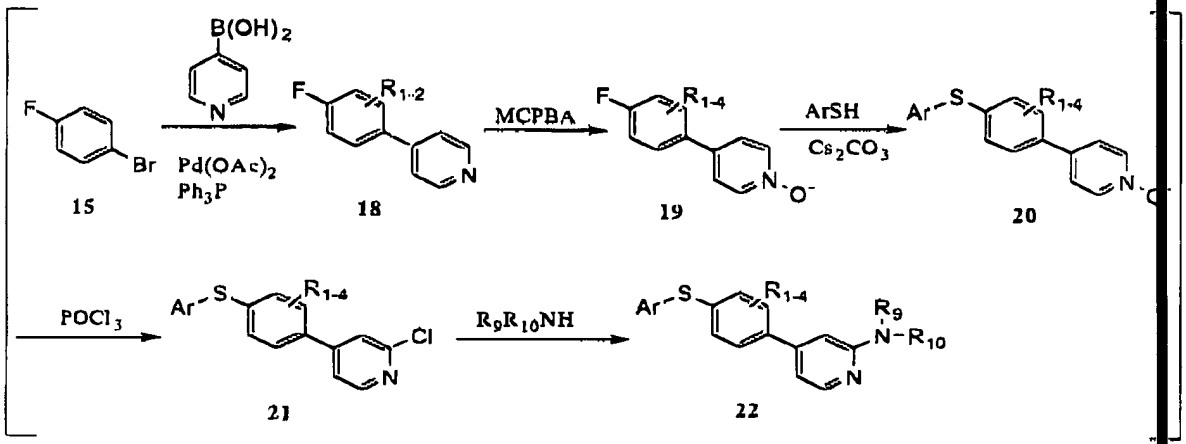
Scheme 5

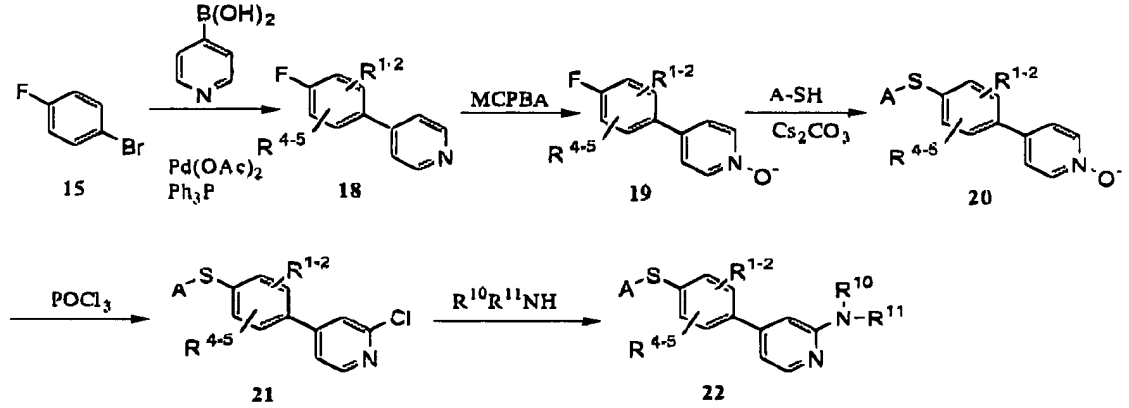


Yet another class of compounds of Formula I are compounds containing a pyridine ring, for example 2,4-disubstituted pyridines (n=1, Y=C, B=N, Z=C, D=C). Scheme 6 describes one procedure for the preparation of this class of compounds. In Scheme 6, [Thus,] Pd-catalyzed cross-coupling of a properly substituted 1-bromo-4-fluoro-benzene **15** and 4-pyridine boronic acid gives compounds **18**. Oxidation of **18** with MCPBA leads to pyridinium oxide **19**. Displacement of the fluoride of **19** with an aryl thio [thiols then] affords biarylsulfide **20**. Treatment of **20** with $POCl_3$, leads to 2-chloropyridine **21**. Finally, reaction

of **21** with a selected amine [amines] gives a [the] desired 2-aminopyridine [2-aminopyridines] **22**.

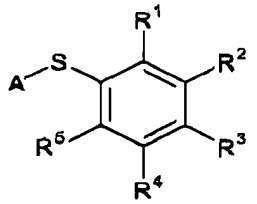
Scheme 6





VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES

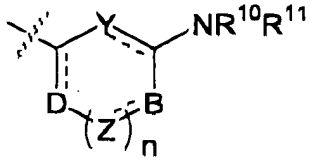
1. (Amended) A compound of [the structure] formula I



I

or a pharmaceutically acceptable salt or prodrug thereof,

wherein R^1, R^2, R^3, R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, [and] carboxaldehyde[;], and a group of formula II defined as



II

subject to [with] the proviso that one or more than [at least] one of R^1 or R^3 is a group of formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of $-CR^6=$, $-CR^7R^8-$, C(O)-, -O-, $-SO_2-$, -S-, -N=, and $-NR^9-$;

n is an integer of zero to three;

R^6, R^7, R^8, and R^9, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl[]alkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

[wherein] R^{10} and R^{11} are taken together with N [may be joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, [said ring being optionally] substituted with one or more than one substitutent [substituents] R^{13}, wherein R^{13}, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

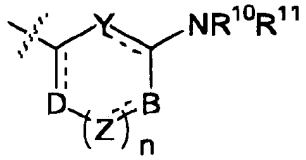
wherein A is an unsubstituted aryl [or] group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than [said aryl or heterocyclyl group having at least] one substituent R^{12}, wherein R^{12}, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamido, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino,

carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl and heterocyclylalkylaminocarbonyl; and

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10},R^{11}, R^{12} and R^{13} are unsubstituted or substituted with one or more than [at least] one electron donating or electron withdrawing group[;]

[or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof].

2. A [The] compound according to [of] claim 1 wherein R^3 is the group of formula II



II

wherein R^{10}, R^{11}, D, B, Y, [and] Z, and n are defined as in claim 1. [at each occurrence are defined as in claim 1 independently selected from the group consisting of $-CR^6=$, $-CR^7R^8-$, C(O)-, -O-, $-SO_2-$, -S-, -N=, and $-NR^9-$;

n is an integer of zero to three;

R^6, R^7, R^8, and R^9, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl;

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

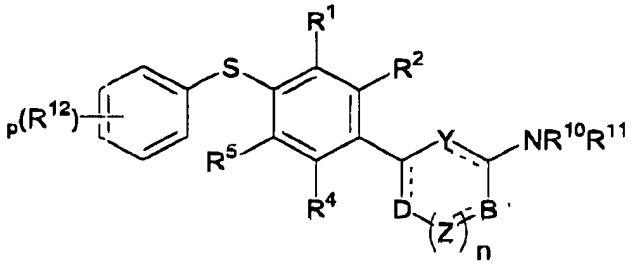
R^{10} and R^{11} may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents R^{13}, wherein R^{13}, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy,

alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, haloalkyl and nitro; and

R^4 and R^5 are each independently selected from the group of hydrogen and alkyl.]

3. (Amended) A [The] compound according to [of] claim 1 of [the structure] formula III



III

wherein R^1, R^2, R^4, R^5, R^{10}, R^{11}, R^{12}, D, B, Y, Z, and n are defined as in claim 1;

[R^1, R^2, R^3, R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

wherein D, B, Y and Z at each occurrence are independently selected from the group

consisting of -CR^6==, -CR^7R^8-, C(O)-, -O-, -SO_2-, -S-, -N=, and -NR^9-;

n is an integer of zero to three;

wherein R^6, R^7, R^8, and R^9, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl alkyl, dialkylaminocarbonylalkyl and carboxyalkyl;

R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

wherein R^{10} and R^{11} may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents R^{13}, wherein R^{13}, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

R^{12}, at each occurrence, is independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;] and

p is an integer of zero to five[;

wherein R^1, R^2, R^4, R^5, R^{10},R^{11}, R^{12}, and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group].

4. (Amended) A [The] compound according to [of] claim 3 wherein p is one;

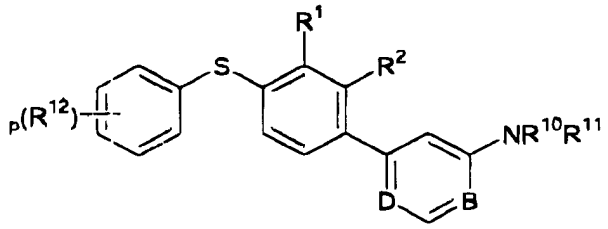
R^4 and R^5 are hydrogen;

R^{12} is selected from the group consisting of halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

R^{10} and R^{11} are taken together with N [joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring[;], substituted with one or more than one substituent [substituents] R^{13}, wherein R^{13} is defined as in claim 1, and wherein said substituted heterocyclyl, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine[.]; and

wherein R^{10}, R^{11}, R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group.

5. (Amended) A [The] compound according to [of] claim 1 of [the structure] formula IV



IV

wherein D and B are each independently selected from the group consisting of -N= and -CR^6=;

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are defined as in claim 1;

[R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

wherein R^{10} and R^{11} may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents R^{13}, wherein R^{13}, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;]

R^{12}, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl, wherein R^{12} is unsubstituted or substituted with at least one electron donating group or electron withdrawing group ; and[,]

p is an integer of zero to five[;

[wherein R^1, R^2, R^{10}, R^{11}, R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating group or electron withdrawing group].

6. (Amended) A [The] compound according to [of] claim 5 wherein p is one;

[R^{12} is selected from the group consisting of halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;] and

R^{10} and R^{11} are taken together with N [joined] to form a three to seven membered

substituted heterocyclyl ring, or a three to seven membered unsubstituted heterocyclyl ring[;], substituted with one or more substituents R^{13}, wherein R^{13} is defined as in claim 1, and wherein said substituted heterocyclyl ring, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine.

7. (Amended) A [The] compound according to [of] claim 1 selected from the group consisting of 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(3-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(4-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-3-yl)-methanol, 2-(1-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyhl-phenyl)-pyrimidin-4-yl)-piperidin-4-yl)-ethanol, *N*-(1-(4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidin-3-yl)-acetamide, 1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)pyridin-2-yl)-pyrrolidine-3-ol, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acetamide, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acedemide, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidin-3-yl)-acetamide, 4'-(4-(2,3-dihydro-benzo(1,4) dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)- 3,4, 5, 6 -tetrahydro-2H-(1,2') bipyridinyl-5-carboxylic acid, and 4'-(4-(2,3-dihydrobenzo (1,4) dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2*H*-(1,2')(bipyridinyl-3-carboxylic acid.

8. (Amended) A composition comprising:

a compound according to [of] claim 1

and [in] a pharmaceutically acceptable carrier.

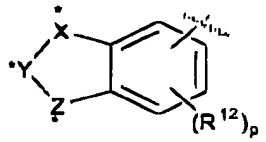
9. (Amended) A method of inhibiting inflammation or suppressing immune response in a mammal comprising administering to said mammal a therapeutic amount of a compound

according to [of] claim 1.

10. (New) A compound according to claim 1 wherein A is

(i) an unsubstituted or substituted aryl group, substituted by one or more than one substituent R^{12}, wherein R^{12} is defined as in claim 1, or

(ii) an unsubstituted or substituted heterocyclyl group of the formula



wherein

R^{12} and is defined as in claim 1;

p is an integer of 0 to 5;

X* and Z* are each independently selected from the group consisting of $-CH_2-$, $-CH_2NH-$, $-CH_2O-$, -NH-, and -O-, with the proviso that at least one of X* and Z* is not $-CH_2-$; and

Y* is $-(C(R")_2)_v-$, wherein

R" is hydrogen or alkyl; and

v is 1, 2, or 3.

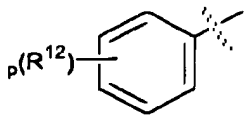
11. (New) A compound according to claim 1 or 10 wherein A is an unsubstituted or substituted aryl group, wherein the aryl group is

a) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings, or

b) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings, wherein one or more than one of the aromatic rings is fused to a ring selected

from the group consisting of cyclohexane, cyclohexene, cyclopentane, and cyclopentene.

12. (New) A compound according to claim 1 wherein A is an unsubstituted or substituted aryl group of the formula



wherein R^{12} is defined as in claim 1; and p is an integer of 0 to 5.

13. (New) A compound according to claim 1 wherein

D is $-CR^6=$ or $-N=$,

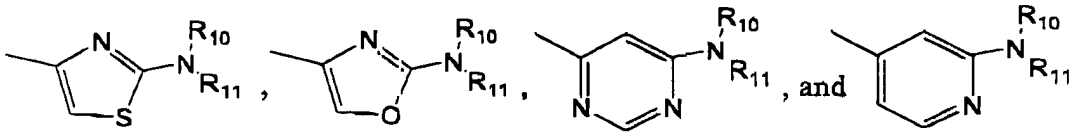
B is -S-, -O-, $-CR^6=$ or $-N=$,

Y is $-CR^6=$ or $-N=$,

Z is $-CR^6=$ or $-N=$; and

n is zero or one.

14. (New) A compound according to claim 1 wherein R^3 is selected from the group consisting of



15. (New) A compound according to claim 1 wherein

D is $-CR^6=$;

B is -O- or -S-;

Y is $-N=$; and

n is zero.

16. (New) A compound according to claim 1 wherein

D is $-CR^6=$ or $-N=$;

B is $-N=$;

Y is $CR^6=$; and

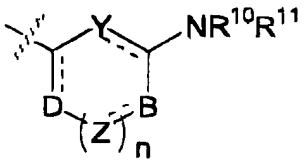
n is 1.

17. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, alkyl, and nitro;

R^4 and R^5 are each independently selected from the group consisting of hydrogen and alkyl; and

R^3 is



wherein

D is $-CR^6=$ or $-N=$,

B is -S-, -O-, $-CR^6=$ or $-N=$,

Y is $-CR^6=$ or $-N=$,

Z is $-CR^6=$ or $-N=$; and

n is zero or one.

18. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl; and

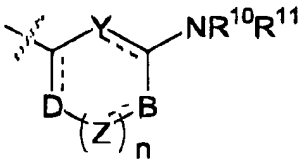
R^4 and R^5 are each independently hydrogen.

19. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is



wherein

D is $-CR^6=$ or $-N=$,

B is -S-, -O-, $-CR^6=$ or $-N=$,

Y is $-CR^6=$ or $-N=$,

Z is $-CR^6=$ or $-N=$; and

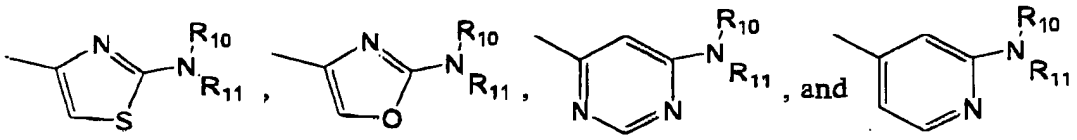
n is zero or one.

20. (New) A compound according to claim 1 wherein

R^1 and R^2 are each independently are selected from the group consisting of hydrogen, chloro, and trifluoromethyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is selected from the group consisting of



21. (New) A compound according to claim 1 wherein R^6 is hydrogen.

22. (New) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl,

R^2 is selected from the group consisting of hydrogen and halogen, and

R^4 and R^5 are each independently hydrogen.

23. (New) A compound according to claim 22 wherein

R^1 is trifluoromethyl, and

R^2 is hydrogen.

24. (New) A compound according to claim 22 wherein R^1 and R^2 are each independently chloro.

25. (New) A compound according to claim 1 which has an IC_{50} of less than 20 μM when tested in one or both of

(i) an ICAM-1/LFA-1 Biochemical Interaction Assay, or

(ii) an ICAM-1/JY-8 Cell Adhesion Assay.

26. (New) A method for ameliorating a pathology in a mammal arising from the interactio of LFA-1 with ICAM-1 or ICAM-3 comprising administering to said mammal a therapeutic amount of a compound according to claim 1.

27. (New) A method according to claim 26 wherein the pathology is selected from an inflammatory disease, an autoimmune disease, tumor metastasis, allograft rejection and reperfusion injury.